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Knee osteoarthritis among airport baggage handlers

A prospective cohort study

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Knee osteoarthritis among airport baggage handlers: **a prospective cohort study**

Short title: Knee osteoarthritis among airport baggage handlers

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Authors' contributions:

LCT, SM and CB had full access to all data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. Conception and design: SM, CB, LCT, TA, EBS. Acquisition, analysis or interpretation of data: All authors. Statistical analysis: LCT. Drafting the manuscript: SM, EBP, LCT, CB. Critical revision of the manuscript for important intellectual content: All authors.

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The study was notified to the Scientific Ethical Committee, The Capital Region of Denmark (journal number H-4-2011-125 and H-3-2012-027). According to Danish law, register-based studies and questionnaire studies need neither approval from ethical and scientific committees nor informed consent.[12] The study was registered at The Danish Data Protection Agency (journal no: 2012-41-0199).

Competing interest:

The authors declare no conflicts of interest.

Disclaimer: *None*

ABSTRACT

Background: Knee osteoarthritis is a common and often disabling disorder, which has been related to knee-straining work. However, exposure response relations are uncertain and there are few prospective studies. We studied prospectively if incident knee osteoarthritis is associated with cumulative exposure as an airport baggage handler, lifting on average 5000 kg per day.

Methods: The study is based on the Copenhagen Airport Cohort, a historical cohort of male baggage handlers and a reference group of unskilled men from the greater Copenhagen area, followed from 1990 to 2012. Cumulative years of employment as a

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baggage handler was based on information from company employment and union registers. Outcome was first hospital admission with a discharge diagnosis of knee osteoarthritis and/or knee replacement, ascertained from the Danish National Patient Register.

Results: The cohort contained 3,442 baggage handlers and 65,511 workers in the reference group. The unadjusted incidence rate ratio (IRR) of knee osteoarthritis increased steeply with cumulative years as a baggage handler. Although the exposure-response pattern became weaker and statistically non-significant ($p \approx 0.10$) when adjusting for age, the risk of knee osteoarthritis was still increased in baggage handlers at the highest exposure level. Additional analyses showed that the association between age and osteoarthritis was stronger for baggage handlers (IRR=2.09; 95%CI: 1.68-2.60) than for referents (IRR=1.58; 1.53-1.63), indicating that knee osteoarthritis occurred at a younger age among baggage handlers than in the reference group.

Conclusions: The results of this prospective cohort study support that long-term heavy lifting increases the risk of knee osteoarthritis.

Keywords: knee osteoarthritis; etiology; occupation; kneeling; squatting, heavy lifting; epidemiology; cohort study; airport baggage handlers

1 INTRODUCTION

Knee osteoarthritis (knee-OA) is a common disorder after the age of fifty and one of the leading causes of disability [1]. Globally, the prevalence of radiographically confirmed symptomatic knee-OA has been estimated to be 3% for men and 4% for women [1]. Knee-

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OA is closely related to age. In the USA, the prevalence among 60+ years old men and women is 10% and 13%, respectively [2]. Other established risk factors are female sex, obesity, knee joint injuries, meniscectomy and inherited predisposition to osteoarthritis [3, 4].

Occupational activities with knee straining work is commonly considered to be a risk factor for knee-OA or aggravation of knee-OA, but the role of duration and intensity of lifting and work positions is not very clear [3-5]. A systematic review by McWilliams et al. considered included studies to be very heterogeneous, and results from case-control and cross-sectional studies were influenced by publication bias [3]. Recently, Verbeek et al. reviewed studies to establish quantitative exposure-response relations for lifting and kneeling. No cohort studies and only five case-control studies qualified for this purpose [5]. Furthermore, the authors assessed the risk of bias as high except for one study.

The risk of biased results in studies of knee-OA and occupational activities is due to several methodological problems [3, 4] among which retrospective exposure assessment and differential attrition seem to be of special concern [5]. Prospective cohort studies are few but have the advantage of defining exposure before the outcome occurs and have therefore been specifically called for to improve the evidence base [3, 6].

We utilized the Copenhagen Airport Cohort [7] in a prospective study of incident knee-OA among airport baggage handlers and an external reference group. We used cumulative time as a baggage handler as a quantitative measure of exposure with newly hired baggage handlers as the reference. Baggage handling in airports is unskilled work characterized by repetitive heavy lifting, frequently under time pressure and partly in awkward positions. Exposure time as a baggage handler was recorded objectively for

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each calendar year, before and independent of the outcome. The outcome was a diagnosis of knee-OA obtained from the Danish National Patient Register. Follow-up over twenty-two years was almost complete. Owing to detailed objective information on generic work-load, the results may be generalizable to other manual lifting work.

2 MATERIAL AND METHODS

2.1 Cohort

The Copenhagen Airport Cohort includes male baggage handlers with former and present employment at Copenhagen Airport (CPH) and a reference group of unskilled male workers with other occupations employed at the airport or in other companies in the Greater Copenhagen area during the period 1990-2012 (n=69,175). Information on employment and work tasks, including entry and exit dates, was recorded from electronic company employment registers and union member registers. All participants were identified by their unique personal identification number.

The reference group had a variety of tasks (e.g. drivers, security, cleaning and maintenance within the airport, and municipal workers, drivers, postal workers, garbage collectors and factory workers outside the airport). We controlled for overlapping information obtained from the different registers. We found good agreement between the data sources, e.g. 87% of persons recorded as baggage handlers by the union were also recorded as baggage handlers in company employment registers. In case of conflicting information we used the company employment information because it was linked to payment of salary and therefore considered as the most reliable and accurate. The cohort is described in more detail in previous publications [7-9].

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By linkage with the personal identification number we followed the cohort in the National Patient Register (NPR), the Civil Registration System and registers at Statistics Denmark to obtain information on diagnoses, surgery, mortality, migration, pensioning, and educational level [10-12].

Self-reported data on work, health, body mass index (weight(kg)/height(m)^2) (BMI), physical activity, drinking and smoking habits were collected by a questionnaire in 2012 [13]. The questionnaire was delivered to all baggage handlers and a random sample of the external reference group who met the following criteria: Alive on April 2012, permanent residence in Denmark, aged 25-75 years and no previous refusal of participating in research projects (an option in the Danish Civil Registration System). Responses were obtained from 3749 out of 5474 men with a response rate of 68.5% for both baggage handlers and referents. Respondents were more often Danish of origin, had a higher education and were more often married than non-responders {Moller, 2017 144 /id}. Since the survey information was collected from a sample of cohort survivors at the end of follow-up these data only served descriptive purposes.

2.2 Exposure

The level of exposure to manual baggage handling was assessed from different sources. We observed the work of baggage handlers during a two-week period and interviewed workers and management about the work, work organization, and changes over time. We scrutinized company employment registers and production statistics for information on work load as well as company occupational health service assessments from 1991, 1998 and 2001. Baggage handlers either worked in the baggage sorting area inside the terminal building or outdoor on the apron where parked aircrafts are loaded and unloaded. In the

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baggage sorting area they loaded or unloaded baggage carts or containers to or from a belt conveyor. The working position was mainly standing, stooping or walking, but bending of the back and knees is not uncommon, and some squatting and kneeling occurred. On the apron they loaded or unloaded most aircraft manually. One baggage handler was standing at the belt loader on the ground, loading and unloading baggage between baggage carts and belt loader, while another was in the baggage compartment, packing and unpacking baggage, often in sitting, kneeling or squatting work positions due to the confined space. Usually one aircraft was loaded or unloaded per hour by a team of 2-4 baggage handlers. This took approximately 25-30 minutes of intensive work, depending on the amount of baggage in the aircraft, and was followed by other duties or a pause until the next handling. Since 2002 and 2009 the two baggage handling companies have kept records on the number of baggage pieces and their total weight for every single flight. This information showed that the average weight of a baggage piece was approximately 15 kg, and the average total amount of baggage lifted in an 8-hour shift is approximately 5000 kg per baggage handler. Other production statistics and occupational health service reports showed that the daily lifting load per baggage handler had been fairly constant since 1990. Lifting equipment in the form of pneumatic lifting hooks was introduced in the baggage sorting area in 1998. Extended and flexible belt loaders were routinely used on the apron from approximately 2004.

Company employment records included information on dates of entry and exit of baggage handling departments, and of departments or work units mainly working in the baggage sorting area or on the apron. Other information on work load could not be used at the individual level.

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Individual exposure was expressed as cumulative years of employment as a baggage handler. We computed the proportion of employment as a baggage handler for each year and then cumulated these proportions year by year during follow-up resulting in a time-dependent measure of cumulative years as a baggage handler for each year. Similarly, we calculated cumulative years of employment separately for work in the baggage sorting area and on the apron, and for employment before and after 1998 and 2004, respectively, to evaluate the influence of the technical aids mentioned above.

2.3 Outcome

The outcome was first hospitalization with knee-OA as the primary discharge diagnosis or surgery for knee-OA. The cohort was linked with the National Patient Register (NPR) which covers all contacts to the secondary health care system with information on dates of admission and discharge diagnoses, and dates of surgery and surgical procedure codes.

Before 1994 all diagnoses were classified according to the International Classification of Diseases version 8 (ICD-8) and from 1994 according to version 10 (ICD-10). Before 1996 surgical procedures were coded according to a Danish classification system, from 1996 they were classified by the NOMESCO classification of Surgical Procedures. The following diagnoses were included: ICD8: knee osteoarthritis (713.01); ICD-10: primary knee osteoarthritis (M17.0, M17.1, M17.1B) and unspecified knee osteoarthritis (M17.9). We further included surgical treatment with partial or total knee replacement classified by the Danish surgical procedures classification before 1996 (codes 70040-70049, 82780, 82800) and from 1996 by the NOMESCO classification of Surgical Procedures (KNGB codes) [14].

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2.3 Confounders

We considered the following factors as potential confounders: age, calendar year, highest attained educational level, pre-employment knee-trauma or -surgery, availability of lifting equipment in the baggage sorting area and extended belt loaders in aircraft baggage compartments.

Age was included categorically (<30, 30-44, 45-59 and 60+ years); calendar year was included categorically (1990-1994, 1995-1999, 2000-2004 and 2005-2012); and educational level by four categories (elementary school, high school, vocational education and higher education). Information about pre-employment knee-trauma and -surgery was obtained from the National Patient Register based on discharge diagnoses of knee luxations, distorsions and traumatic lesions of ligaments and menisci (ICD-8: 836, 844, 849.40–849.49; ICD-10: S83) and surgical procedures on the knee joint, ligaments and capsule (Danish surgical procedure classification codes before 1996: 71540 to 74549 for the knee region; NOMESCO codes from 1996: groups NGA to NGK). The use of lifting equipment in the baggage sorting area and extended belt loaders on the apron were included as binary covariates (no/yes for work before/after 1998 in the baggage sorting area, and no/yes for work before/after 2004 on the apron, respectively)

As descriptive measures we report distribution statistics for questionnaire information on BMI, leisure time physical activity, smoking habits, alcohol consumption and sport activities, knee pain during the past 12 months, and for baggage handlers also self-reported information about work on the apron.

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2.4 Statistical analyses

From the cohort of 69,175 persons we excluded persons with an outcome before first date of employment leaving 68,953 persons in the cohort. They were followed from start of first employment,

January 1990 or immigration after employment, whichever came last, and until first diagnosis or surgery for knee-OAs, emigration, death or end of follow-up (31 December 2012), whichever came first.

The effect of baggage handling was examined in four preselected models with the following baggage handling covariates:

1) Baggage handlers compared to the external reference group. To be comparable with the results of the other models, the baggage handler group was used as the reference, see below.

2) Baggage handler cumulative years categorical (0.1-2.9 years, 3.0-9.9 years, 10.0-19.9 years, and 20+ years). The external reference group was included as a category. The baggage handler group with 0.1-2.9 years cumulative exposure served as reference group because the internal exposure response associations are simpler described with this parametrization than by using the external reference group as the reference.

3) Cumulative years as a continuous variable and including the binary group variable, coded '1' for the external reference group and '0' for baggage

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handlers. By this coding, the effect of cumulative years only refers to baggage handler cumulative years.

4) Cumulative years as a restricted cubic spline with knots at 5th, 27.5th, 50th, 72.5th, and 95th percentiles of the distribution of cumulative years. We used the PSPLINET macro. In this model we included the same binary group variable, so the effect of cumulative years only refers to baggage handler cumulative years. Model 4 included test for non-linearity of the influence of cumulative years on knee-OA using the likelihood ratio test, comparing the model with only the linear term to the model with the cubic spline terms.

The analyses were performed unadjusted and adjusted for potential confounders.

Cumulative years and age were strongly correlated (Pearson's correlation coefficient, 0.63) and age had a strong effect on knee-OA (see below). We did three additional analyses to assess the relative importance of cumulative years and age and if adjustment for the strong effect of age introduced an over-adjustment of effects of cumulative exposure:.

1) We analysed the adjusted models with all confounders except age.

2) To reduce the collinearity among cumulative years and age, we computed residuals from a linear regression of cumulative years on age. The resulting residuals were used for age-adjustment and modeled as a linear term.

3) We evaluated the influence of age without adjustment for cumulative years, separately for baggage handlers and the external reference group, and tested

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the interaction between age and status as a baggage handler, adjusted for the other confounders.

We also estimated the influence of cumulative years in the baggage sorting area and on the apron, total and split into periods before and after introduction of technical aids in 1998 and 2004, respectively. These analyses were also made according to model 1 to 3 as described above, except that categories of cumulative years had to be changed to get an acceptable number of cases of knee-OA in each category of cumulative years. Finally, we evaluated the influence of years since employment termination in a model adjusted for confounders and cumulative years. The influence of years since termination was modelled as a restricted cubic spline and as a linear effect. We also tested whether there was an interaction between cumulative years and years since termination included as linear effects. Due to the change in diagnostic classification system in 1994 we made a parallel set of analyses for outcomes that occurred after January 1st, 1994.

Two-sided p values below 0.05 were considered statistically significant. Data were analyzed using Poisson regression with log-transformation of person-years at risk and Cox regression (restricted cubic splines) using SAS version 9.3 (SAS Institute Inc., Cary, North Carolina, USA).

2.5 Ethics

The study was approved by The Danish Data Protection Agency (journal no: 2012-41-0199). The study was notified to the Scientific Ethical Committee, The Capital Region of Denmark (journal number H-4-2011-125 and H-3-2012-027). According to Danish law, register-based studies and questionnaire surveys do not need approval from ethical and

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scientific committees or informed consent.[12] Individual participant anonymity is secured by the research platform of Statistics Denmark. Questionnaires were accompanied by a letter of information on the purpose of the study and how anonymity of data was secured, and written informed consent is therefore implied by returning a filled questionnaire.

3 RESULTS

The cohort consisted of 3,442 baggage handlers and 65,511 referents at risk of a first-time diagnosis of knee-OAs (Table 1). The baggage handlers were younger at entry to the cohort and they had a vocational education more often than the external reference group. Self-reported data from 2012 showed that BMI, smoking, alcohol consumption and physical activity were comparable between baggage handlers and reference group. Baggage handlers reported knee pain more often (23% vs. 15% in the reference group). Almost 70 % of the baggage handlers reported, that on the apron they worked equally on the ground and in the baggage compartment. When they worked in the baggage compartment 18% reported that they worked in a kneeling position more than 50% of the time.

There were 1,862 incident cases of knee-OA, 1,792 referents and 70 baggage handlers. The incidence rate of knee-OA was slightly higher among referents compared to baggage handlers but the difference was not statistically significant (Table 2, model 1).

The unadjusted incidence rate ratio (IRR) of knee-OA increased with longer cumulative years of employment as a baggage handler and was significantly higher for baggage handlers with 10-19 and ≥20 cumulative years compared to baggage handlers with 0-<3

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cumulative years (Table 2 model 2). After adjustment for potential confounders this pattern remained but became weaker and the difference between baggage handler exposure groups was no longer statistically significant (p=0.11). However, the IRR for baggage handlers with ≥20 cumulative years was still statistically significantly higher than for baggage handlers with 0-<3 cumulative years (IRR= 2.18 (95% confidence interval (CI): 1.01 - 4.70). The results were similar in analyses of cumulative years as a continuous variable with a linear effect (Table 2 model 3). In this model, the adjusted IRR was 1.11 (95% CI: 0.98-1.26) for each five years increase in cumulative years.

The restricted cubic spline analyses with cumulative years as a continuous variable showed an increasing incidence of knee-OA among baggage handlers during the first 10 to 15 cumulative years and then decreased slightly in the fully adjusted model. If age was not included in the adjustment (see below) the association with cumulative years was stronger and continued to increase at a lower rate after 15 cumulative years (Figure 1). The test for non-linearity was non-significant in both analyses (p=0.53 (fully adjusted), p=0.24 (fully adjusted except for age)) indicating that the association may be adequately described by the simpler linear model (Table 2, model 3).

In the analyses of the relative importance of cumulative years and age we first excluded age from the fully adjusted model. In this analysis the associations of cumulative years with knee-OA were similar to the unadjusted associations (Table 3-adj2 model). A similar result was found when adjustment for age was restricted to the residual age term ((Table 3-adj3 model). These results demonstrate that the differences between the results of the unadjusted and the fully adjusted analyses were mainly due to the collinearity between age and cumulative years as a baggage handler.

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The association between age and knee-OA was very strong. The incidence rates per 10,000 person-years for age groups 30-44, 45-59 and 60+ were 7.24, 21.3 and 30.0 times higher than for the age group below 30 years of age (adjusted for other covariates in model 2). The association between age and knee-OA was stronger for baggage handlers than for referents. An increase by 10 years of age was associated with IRR=2.09 (1.68-2.60) for baggage handlers and IRR=1.58 (1.53-1.63) for the reference group, adjusted for the other confounders. This difference was statistically significant (p=0.01). Furthermore, the effect of the residual age term among baggage handlers was similar to the effect age among the referents, indicating that there would have been no difference in the effect of age in the two groups if effects of baggage handler cumulative years was subtracted from the effects of age among baggage handlers.

In the separate analyses of work in the baggage sorting area there was a positive association between cumulative years worked in this area and knee-OA, total for all years (linear effect of five years : IRR=1.18 (95% CI: 0.92-1.52), p=0.19)), and for work before 1998 (linear effect of five years: IRR=1.32 (95% CI: (0.99-1.76)), p=0.06), but not for work after 1998 (IRR=0.83 (95% CI: 0.38-1.80, p=0.63). Similar results were found for work on the apron, total for all years (linear effect of five years: IRR=1.13 (95% CI: (0.96-1.33), p=0.14)), and for years worked before 2004 ((linear effect of five years: IRR=1.16 (95% CI: (0.98-1.37), p=0.09)), but not for work after 2004 (IRR=0.86 (95% CI: 0.44-1.70, p=0.66).

The influence of time since termination of employment showed a linear decreasing trend (the test for nonlinearity was non-significant (p=0.13)) with a hazard ratio of 0.71 (95 %

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CI: 0.45-1.12; p=0.15) for every five years since termination. There was no interaction between time since termination and cumulative years of employment (p = 0.80).

The results from the sensitivity analyses of only outcomes that occurred after the change in diagnostic coding system in 1994 were very similar to the results presented above.

4 DISCUSSION

The risk of developing knee-OA increased with cumulative years of baggage handling. This relation was statistically highly significant in unadjusted analyses and in adjusted analyses if age was not included in the adjustment, or if age was only included as residuals of age regressed on cumulative years. When age was included the exposure-response pattern remained but became weaker and statistically non-significant ($p \approx 0.10$), but the incidence rate of knee-OA was still significantly higher in the highest exposure group compared to the lowest exposure group. The strong confounding effect of age was also illustrated in the spline curves. Separate analyses of knee-OA in relation to cumulative years of work in the baggage sorting area and on the apron showed results similar to the main analyses for both types of work for the periods before technical baggage handling aids were introduced, but not after. Furthermore, the effect of age was significantly stronger among baggage handlers than among referents. The risk of knee-OA tended to decline after cessation of work as a baggage handler but not significantly so.

Age had a much stronger association with knee-OA than cumulative years as a baggage handler, and also had a strong association with cumulative years. Part of the stronger association of age to knee-OA may be due to a relatively larger variation of age than of

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cumulative years, since age continues to exert its adverse effects on the knees in the years after cessation of work. Furthermore, age was measured precisely while cumulative years included some misclassification and may not be complete back in time. In this situation it was not possible to separate the independent association of cumulative years with knee-OA from that of age.

We consider the association between cumulative years and knee-OA as overadjusted by age and therefore biased towards unity. Misclassification and lack of precision of the exposure measure will also bias risk estimates towards unity. Despite these biases, age adjusted risk estimates showed a consistent exposure-response relation approaching statistical significance; baggage handlers with the highest level of cumulative exposure had a statistically significantly higher risk of knee-OA than baggage handlers with the lowest level; technical lifting aids seemed to lower the risk of knee-OA; and the effect of age was statistically significantly stronger among baggage handlers than among referents. Altogether, we find it unlikely that this pattern of associations is due to chance.

4.1 Exposure

Exposure status and cumulative exposure was based on objective information recorded independently of the outcome. This information allowed the construction of a well-defined cohort of baggage handlers and the calculation of individual cumulative time as a baggage handler based on the annual number of days with baggage handling for many years back in time. Overall, there was a fairly good accordance between union and employment registers with respect to status as a baggage handler, e.g. 87% of persons

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recorded as baggage handlers by the union were also recorded as baggage handlers in the company employment records [7], and 84% of baggage handlers that responded to the survey in 2012 confirmed that they worked or had worked as baggage handlers [13].

However, some exposure misclassification occurred. Status as a baggage handler was defined as unskilled work in baggage handling departments and included some workers with mostly other work tasks in these departments (e.g. tractoring aircraft, deicing, special services etc.). Furthermore, there is some uncertainty with respect to the completeness of transfer of data from manual registers to electronic registers back in time (for details see [7], and there has also been some misclassification with respect to working with baggage sorting or on the apron. We only have individual data on working days as a baggage handler, whereas data on lifting and work positions are all based on averages or a general description. Thus, although handling only involves relatively few and homogeneous work tasks, cumulative years as a baggage handler is a crude measure of knee-straining work. These misclassifications are most likely non-differential and will therefore bias the results towards the null.

We chose a reference group of unskilled workers to reduce confounding from socioeconomic differences. This choice reduced the exposure contrast between the two groups because many unskilled workers have some knee straining work tasks. However, we are confident that there was a significant contrast in knee-straining work between the two groups since only few unskilled workers lift an average of 5000 kg per day.

The similar risk in the two groups may possibly be explained by a combination of reduced contrast, some misclassification of status as baggage handler, overadjustment by

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age, a healthy worker effect and residual confounding related to socioeconomic status (SES).

The exposure contrast related to different working position in the baggage sorting area and on the apron was attenuated because loading and unloading aircraft constituted only approximately half of the working day, and work on the apron was approximately equally divided between working in the aircraft baggage compartment in awkward positions and on the ground in work positions similar to those in the baggage sorting area. Based on baggage handler self-reports on work on the apron (Table 1) we estimate that the average time spent in a kneeling position when working on the apron amounts to approximately 45 minutes per day, however with a large variation. Whether this is sufficient exposure to kneeling to increase the risk of knee-OA is uncertain.

The within baggage handler exposure contrast for cumulative exposure was good, varying from >0 to 40 cumulative years.

4.2 Selection

Most likely, persons recruited into physically demanding jobs are fitter and have less joint problems, than persons who choose other jobs, and if joint problems occur they may leave the job more often than persons in less demanding jobs. This healthy hire and survivor selection may have biased our results for group comparisons towards the null, and a healthy survivor selection could similarly affect the results for cumulative exposure. The younger age of baggage handlers compared to referents could be related to the greater fitness demands for baggage handlers but may also be due to registration differences since baggage handlers were primarily included from company employment

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registers and referents primarily from union registers. Furthermore, baggage handlers were better educated with a lower proportion with only elementary school and a higher proportion with vocational education than the referents. This difference may reflect a selection related to attractive aspects of employment as a baggage handler, including better wages and a well-organized and influential worker organization at the work place. We adjusted for educational level but cannot exclude residual SES-related confounding that could bias group comparisons towards the null, but most likely not results based on cumulative exposure.

4.3 Outcome

Our outcome was first hospital discharge diagnosis of knee-OA in the Danish National Patient Register. The register is quite complete and of high quality [10]. It is unlikely that a discharge diagnosis of knee-OA is made without radiographic confirmation.

Workers with a certain degree of pathoanatomic knee-OA may have more knee symptoms if they are exposed to knee-straining activities and may therefore seek health care, including hospital assessment and treatment, more readily than workers in less demanding jobs, leading to earlier diagnosis. This detection or referral bias may lead to inflated risk estimates for study groups with knee-straining work compared to referents with less knee-straining work [3, 4, 15]. This potential bias seemed less important in our study, or may have been counteracted by factors causing bias towards the null, since the risk of knee-OA was similar for baggage handlers and referents. It seems unlikely that selective referral would vary across cumulative years as a baggage handler and bias risk estimates of cumulative years.

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Our outcome is a fairly advanced degree of knee-OA, because persons with few symptoms will not be referred to hospital assessment and treatment. Approximately 45% of persons with radiographic signs of knee-OA have few or no knee complaints [16], and our results may not be generalizable to such milder degrees of knee-OA.

4.4 Confounding

Associations between measures of exposure and knee-OA were adjusted for age, educational level, calendar year and pre-employment knee-trauma or -surgery, including sport related lesions. We were not able to control for obesity, participation in knee-straining sports, knee abnormalities or generalized osteoarthritis. However, the baggage handlers and referents seemed comparable with respect to body mass index and lifestyle factors (Table 1).

4.5 Other cohort studies

Other Scandinavian prospective studies based on register data and hospital diagnoses of knee-OA have reported an increased incidence of knee-OA in relation to high levels of knee-straining work assessed by occupational title [17-20] or by self-report at baseline [21]. However, the relation was only statistically significant for sub-cohorts in some studies [19, 20]. The effect of cumulatve exposure was only examined in two studies: one found a statistically significant association [17], the other did not [19]. For studies, that compare the incidence of knee-OA diagnosed in the health care system for groups with different knee-straining work, a positive association may reflect that knee-straining work causes or aggravates pathoanatomic knee-OA and/or aggravates symptoms from pathoanatomic

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knee-OA. It seems less likely that effects of cumulative exposure among workers with similar intensity of knee-straining work would be influenced by symptom aggravation.

Other cohort studies were based on a clinical knee-OA diagnosis without radiological confirmation [22, 23], or on radiographic knee-OA [24-26]. All of these studies had high attrition rates. Furthermore, exposure was assessed retrospectively in two studies [25, 26] and two studies examined only the prevalence of the outcome at follow-up and not the incidence from baseline to follow-up [23, 24]. Most prospective cohort studies did not report or had no, little or only circumstantial information on the stability of baseline exposures during follow-up [18-24]. Finally, the results of studies that compare manual with non-manual workers or with the general population may reflect an effect of SES rather than an effect of knee-straining work, or the results could be biased by uncontrolled SES effects [17-19]. Even studies of a wide range of occupations using job exposure matrices or self-reports to establish generic exposures such as lifting and bending are sensitive to SES-confounding because exposures are tightly associated with SES [21-26].

No prospective studies have contributed with reliable quantitative exposure information [5]. Assuming a linear relationship between cumulative exposure and knee-OA and an IRR=1.11 per five years of cumulative exposure (Table 2) implies that the incidence of knee-OA increases by approximately 2% per year when lifting 5000 kg per day of items with an average weight of 15 kg. In a metaanalysis of two case-control studies Verbeek et al. used a unit of 100.000 kg of “lifetime lifting” to assess the risk of knee-OA and found no significant effect (OR=1.00, 95% CI 1.00-1.01). However, it is unclear, what “lifetime” refers to and how the estimate was derived, but the very narrow confidence limits indicate that the unit of exposure was much too small for a sensible estimate. It

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corresponds to 20 days of baggage handler work, which would also result in an IRR=1.00 after rounding. This metaanalysis also estimated that the odds of knee-OA increased 1.26 times with an increase of 5,000 hours of kneeling (based on 5 studies of moderate quality, according to the authors) [5]. To accumulate this exposure for baggage handlers working on the apron would on average take approximately 30 years. However, all of these quantitative exposure estimates are probably quite inaccurate.

4.6 Strengths and limitations

The major strengths of this study are the prospective study design, a large and well-defined cohort with long and almost complete follow-up, and objective and independent measures of exposure and outcome.

The main limitations are misclassification of exposure and difficulties to separate the effect of cumulative exposure from that of age. Furthermore, the results may not be generalized to less severe or radiographic knee-OA. A further limitation was a relatively low number of incident knee-OA cases

5 CONCLUSION

In conclusion, the results of this large prospective cohort with independent objective measures of exposure and outcome and almost complete follow-up support that long-term heavy lifting increases the risk of knee-OA.

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TABLE 1. Characteristics of baggage handlers and the reference group, at baseline for register-based factors, and by 2012 for self-reported factors.

	Baggage handlers		Reference group	
	N	%	N	%
Register-based factors				
Participants total	3442	100	65 511	100
Age groups (years)				
<30	2120	61.6	30 155	46.0
30-44	1205	35.0	21 333	32.6
45-59	115	3.3	10 167	15.5
60+	2	0.1	3856	5.9
Educational level				
Elementary school	1567	45.5	37 114	56.7
High school	442	12.8	8 469	12.9
Vocational education	1285	37.3	16 645	25.4
Higher education	148	4.3	3 283	5.0

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Knee lesions or injury before employment	282	8.2	3 775	5.8
Self-reported factors				
Respondents total	1772	100	1968	100
Body mass index (kg/m^2)				
<18.5	1	0.1	9	0.5
18.5-24.9	602	34.4	686	35.4
25-29.9	861	49.2	897	46.3
30.0+	287	16.4	344	17.8
Smoking				
Never	675	38.4	682	34.8
Past	603	34.3	675	34.5
Current	480	27.3	600	30.7
Alcohol consumption (units/week)				
None	430	24.6	505	25.9
1-21	1240	70.8	1321	67.7
>21	81	4.6	124	6.4
Leisure time physical activity				
Sendentary	173	9.9	254	13.1

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Low	622	35.5	698	35.9
Medium	704	40.2	710	36.5
High	251	14.3	282	14.5
Knee pain during the last 12 months				
Not at all/a little/somewhat	1368	77.2	1669	84.8
Quite a lot/very much	404	22.8	299	15.2
Work on the apron			NA[1]	
Mostly in the baggage compartment	335	22.9		
Equally in the baggage compartment and on the ground	1023	69.8		
Mostly on the ground	107	7.3		
Work position in the baggage compartment			NA[1]	
Standing >25% / 50% of time	76 / 11	4.3 / 0.6		
Stooped >25% / 50% of time	109 / 4	6.2 / 0.2		
Squatting >25% / 50% of time	289 / 19	16.3 / 1.1		
Kneeling >25% / 50% of time	1035 / 312	58.4 / 17.6		
Sitting >25% / 50% of time	670 / 127	37.8 / 7.2		

[1]NA: not applicable

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TABLE 2. Associations of knee osteoarthritis with status as a baggage handler and cumulative years as a baggage handler, Copenhagen Airport Cohort, 1990-2012

Model		Cases	Person-years	IR	IRR (unadj) 95% CI	IRR (adj) 95% CI
1	*Baggage handler*[1]					
	No	1792	987695.1	181.4	1.24 (0.98-1.58)	1.14 (0.70-1.85)
	Yes	70	47947.2	146.0	1.00 (ref)	1.00 (ref)
	p-value				0.075	0.60
2	*Baggage handler cumulative years, categorical*[1]					
	Non-baggage handler	1792	987695.1	181.4	2.71 (1.50-4.90)	1.71 (0.83-3.54)
	0.1-2.9 years	11	16416.8	67.0	1.00 (ref)	1.00 (ref)
	3.0-9.9 years	19	16435.4	115.6	1.73 (0.82-3.63)	1.43 (0.68-3.01)
	10.0-19.9 years	23	10737.6	214.2	3.20 (1.56-6.56)	1.87 (0.91-3.85)
	≥20.0 years	17	4357.4	390.1	5.82 (2.73-12.43)	2.18 (1.01-4.70)

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	p-value[2]	<.0001	0.11
3	*Baggage handler cumulative years, linear*[1]		
	Baggage handler No	2.31 (1.56-3.40)	1.39 (0.81-2.41)
	Yes	1.00 (ref)	1.00 (ref)
	Continuous linear (per 5 years)	1.36 (1.20-1.54)	1.11 (0.98-1.26)
	p-value	<.0001	0.10

Abbreviations: CI, confidence interval; IR, incidence rate per 100,000 person-years; IRR, incidence rate ratio.

[1] Adjusted for age (categorical), use of baggage lifter, use of extendable belt loader, educational level, calendar year and pre-employment knee injury.

[2] p-value of a difference between baggage handler groups (d.f.=3).

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TABLE 3. Different Models for Handling Collinearity between Cumulative Years and Age for the Association between Cumulative Years and knee osteoarthritis, Copenhagen Airport Cohort, 1990-2012

Model		IRR (unadj)	IRR (adj1)[1]	IRR (adj2)[2]	IRR (adj3)[3]
1	*Baggage handler*				
	No	1.24 (0.98-1.58)	1.14 (0.70-1.85)	1.62 (0.99-2.65)	NA
	Yes	1.00 (ref)	1.00 (ref)	1.00 (ref)	
	p-value	0.075	0.60	0.056	
2	*Baggage handler years, categorical*				
	Non-baggage handler	2.71 (1.50-4.90)	1.71 (0.83-3.54)	3.36 (1.63-6.91)	NA
	0.1-2.9 years	1.00 (ref)	1.00 (ref)	1.00 (ref)	1.00 (ref)
	3.0-9.9 years	1.73 (0.82-3.63)	1.43 (0.68-3.01)	1.97 (0.94-4.15)	1.76 (0.84-3.71)

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	10.0-19.9 years	3.20 (1.56-6.56)	1.87 (0.91-3.85)	3.78 (1.84-7.77)	3.13 (1.52-6.47)
	20.0+ years	5.82 (2.73-12.4)	2.18 (1.01-4.70)	6.41 (2.98-13.8)	5.74 (2.64-12.5)
	p-value[4]	<.0001	0.26	<.0001	<.0001
3	*Baggage handler years, linear*[5]				
	Baggage handler No	2.31 (1.56-3.40)	1.39 (0.81-2.41)	2.61 (1.52-4.48)	NA
	Yes	1.00 (ref)	1.00 (ref)	1.00 (ref)	
	Cont. linear (per 5 years)	1.36 (1.20-1.54)	1.11 (0.98-1.26)	1.37 (1.21-1.55)	1.43 (1.25-1.64)
	p-value	<.0001	0.10	<.0001	<.0001

[1] Adjusted for age (categorical), use of baggage lifter, use of extendable belt loader, educational level, calendar year and pre-employment knee injury.

[2] Same adjustment as adj1 but not including age.

[3] Same adjustment as adj2 plus the residuals of linear model (age = cumulative employment years) (see text). These models only include baggage handlers.

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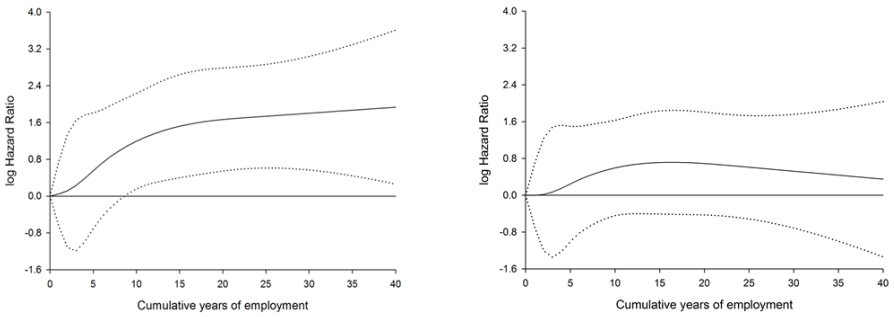
[4] p-value of a difference between baggage handler groups (d.f.=3).

[5] Also adjusted for baggage handler (yes/no).

FIGURE 1. Association between cumulative years of employment as baggage handler and knee osteoarthrosis, Copenhagen Airport Cohort, 1990-2012, restricted cubic splines. Cox regression model. Left panel: adjusted for use of baggage lifter, use of extendable belt loader, educational level, calendar year, pre-employment knee injury and baggage handler (yes/no). Right panel: additional adjustment for age. Dotted lines represent 95% confidence intervals.



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